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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/635,974	08/09/2000	Thomas Teufel	381-86	5643

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EXAMINER
HUNT, JENNIFER ELIZABETH

ART UNIT	PAPER NUMBER
1642	12

DATE MAILED: 05/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No. 09/635,974	Applicant(s) TEUFEL, THOMAS	
	Examiner Jennifer E Hunt	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-43 is/are pending in the application.

4a) Of the above claim(s) 8-43 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 1-7 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 10, 11 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-7, and the species EGFR/HER1, EGF, antibody, and psoriasis in Paper No. 9 is acknowledged. The traversal is on the ground(s) that there is no undue search burden. This is not found persuasive because as set forth in the original restriction requirement, the inventions are not co-extensive and require different grounds of search and consideration.

The requirement is still deemed proper and is therefore made FINAL.

2. The species EGFR/HER1, EGF, antibody, and psoriasis have all been found in the prior art and thus the search has not been extended.

3. Claims 1-43 are pending in the application. Claims 8-43 have been withdrawn from consideration as being drawn to a non-elected invention. Claims 1-7 are pending in the application and considered herein.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating psoriasis using the monoclonal antibody c225, does not reasonably provide enablement for a method of treating the hyperproliferative disease stimulated by a ligand of a member of the epidermal

growth factor family of receptors by administering an antagonist of the EGF family member. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining scope and enablement are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented in the specification, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the predictability of the unpredictability of the art, and 8) the breadth of the claims (see Ex parte Forman, 230 USPQ 546, BPAI, 1986).

The claims are broadly drawn to a method of treating the hyperproliferative disease stimulated by a ligand of a member of the epidermal growth factor family of receptors by administering an antagonist of the EGF family member.

The specification discloses treatment of a single patient who has colon cancer and psoriasis with a combination of cisplatin and c225, and that the patients psoriasis was treating by the protocol.

The specification fails to provide any additional guidance or working examples that other EGFR family members, other antagonists, or other disorders would be subject to the same treatment efficacy instantly exemplified. No mechanism of action is taught or suggested, and no guidance is provided as to rational design for antagonists of other EGFR ligand stimulated disorders.

Disclosure of treatment of a single condition in a single patient using a single specific treatment protocol is insufficient support for claims which are broadly drawn to a method of treating any hyperproliferative disorder using any antagonist of any EGF receptor. The courts have held that:

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based In some way on his teachings, since some improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence, not In compliance with the first paragraph of U.S.C. 112; that paragraph requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill In the art; In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement In the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; In cases involving unpredictable factors, such as chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved." In re Fisher 427 F.2d 833, 166 USPQ 18 (CCPA 1970)

The art of in vivo treatment is complex and unpredictable. Articles by Dillman et al. (*J Clin Onco Vol 12, No 7, pages 1497-1515, 07/1994)* and *Dermer (BIO/TECHNOLOGY, Vol 12, page 320, 03/1994*) are cited in order to establish the

general state of the art and the level of predictability of in vivo therapy . Dillman et al, while discussing observations related to antibody therapy, teach that "on the negative side is the observation that clinical results do not necessarily improve when humanized chimeric antibodies are used in humans, to spite encouraging in vitro results in CDC or ADDC" (page 1506, col 2 paragraph 3). Dermer teaches that "What is significant in culture, for example immunotherapy's killing power or the transformation of 3T3 cells by a mutated proto-oncogene, simply does not have the same significance for cells in vivo."

Therefore in light of the breadth of the claims, the lack of guidance and working examples in the art, the unpredictable nature of the art of cancer treatment, one of skill in art would not be enabled to practice the full scope of the invention.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1-3 and 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bassat et al., Current Pharmaceutical Design, Volume 6, pages 933-942, June 2000, in view of Varani et al., Pathobiology, Vol. 66, pages 253-259, 1998 (IDS).

Bassat et al. teaches a method of treating the hyperproliferative disease stimulated by a ligand of a member of the epidermal growth factor family of receptors (psoriasis, which is stimulated by TGFα, which is the ligand of EGFR) by administering an antagonist of the EGF family member (AG 1571, which inhibits EGFR) to a patient in need thereof (see abstract, and page 934, column 1, and pages 937-940.)

Bassat et al. fails to teach administering an anti-EGFR antibody as the EGFR antagonist.

Varani et al. teaches that anti-EGFR monoclonal antibodies can be used as EGFR antagonists in vitro to treat psoriasis (see page 257.)

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to combine the method of treating psoriasis in patients by administering an anti-EGFR antagonist as taught by Bassat et al., and the anti-EGFR antibody, as taught by Varani et al., and one would have been motivated to do so because anti-EGFR antibodies are effective for treating psoriasis in vitro, as taught by Varani et al.

8. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Varani et al., Pathobiology, Vol. 66, pages 253-259, 1998 (IDS), in view of Goldstein et al., WO 96/40210, published December 19, 1996.

Varani et al. a method of treating the hyperproliferative disease stimulated by a ligand of a member of the epidermal growth factor family of receptors (psoriasis,

which is stimulated by TGFα, which is the ligand of EGFR) by administering an anti-EGFR monoclonal antibody in vitro (see page 257.)

Varani et al. fails to teach that EGFR antibodies can be used for treatment in a patient, that the antibody can be chimeric or humanized, and that the antibody inhibits EGFR/HER1 phosphorylation.

WO 96/40210 discloses the EGFR antibody c225, which is an effective EGFR antagonist in humans. WO 96/40210 also discloses that c225 inhibits EGFR/HER1 phosphorylation, and is more effective for treatment when it is humanized (see for example abstract, and page 14.)

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to use the methods of treating psoriasis by administering an EGFR antibody as taught in Varani in humans, using the humanized anti-EGFR antibody c225, as taught by WO 96/40210, and one would have been motivated to do so because EGFR antibodies are known to be effective in vivo in humans as taught by WO 96/40210.

9. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bassat et al., Current Pharmaceutical Design, Volume 6, pages 933-942, June 2000, in view of Varani et al., Pathobiology, Vol. 66, pages 253-259, 1998 (IDS), and further in view of Goldstein et al., WO 96/40210, published December 19, 1996.

Bassat et al., and Varani et al. teach as applied to claims 1-3 and 6-7 supra. Bassat et al., and Varani et al. fail to teach an anti-EGFR monoclonal antibody which is chimeric or humanized, and which inhibits EGFR/HER1 phosphorylation.

WO 96/40210 discloses the EGFR antibody c225, which is an effective EGFR antagonist in humans. WO 96/40210 also discloses that c225 inhibits EGFR/HER1 phosphorylation, and is more effective for treatment when it is humanized (see for example abstract, and page 14.)

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to use the methods of treating psoriasis by administering an EGFR antibody as taught in Bassat et al., and Varani et al., using the humanized anti-EGFR antibody c225, as taught by WO 96/40210, and one would have been motivated to do so because EGFR antibodies are known to be effective in vivo in humans as taught by WO 96/40210.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E Hunt whose telephone number is (703) 308-7548. The examiner can normally be reached on Monday-Friday, 6-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned

are (703) 305-3014 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0196.

Jennifer E Hunt
Examiner
Art Unit 1642

jeh
May 20, 2002

Sheela G. Huff
SHEELA HUFF
PRIMARY EXAMINER